Criteria-for-Use Checklist Vardenafil non-Responders

VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel

The following criteria-for-use are based on current medical evidence, existing clinical practice guidelines and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient situation.

Vardenafil (Levitra) is the phosphodiesterase type 5 (PDE5) inhibitor on the VA's National Formulary for the treatment of erectile dysfunction. Like many other drug classes such as the NSAIDs, SSRIs, and triptans, individual response may vary within the drug class. At this time, information on rates of response to a second PDE5 inhibitor once a patient has been identified as a non-responder to another PDE5 inhibitor is limited. One vardenafil study (N=449) exclusively enrolled sildenafil non-responders and reported that 65% and 51% of men randomized to vardenafil experienced success based on the SEPQ2 and SEPQ3, respectively compared to the placebo group (33% and 20%, respectively). At the end of the 12 week trial, 31% of men in the vardenafil group had a normal ED score vs. 6% on placebo, and 68% had moved up at least one category on the ED scale vs. 31% on placebo. It should be pointed out that there was no re-challenge with sildenafil as part of demonstrating non-response[1].

The European Association of Urology (EAU) has published guidelines on erectile dysfunction which includes an algorithm that addresses inadequate treatment outcomes[2] The EAU guidelines recommend that when a patient fails one PDE5 inhibitor the following should be addressed before changing treatment: 1) the treatment be assessed for adequate use, 2) the patient is provided adequate instruction and counseling on the use of the product; and 3) the patient has a retrial of at least 4 doses of the original treatment. Patients who continue to have an inadequate outcome should have a trial of at least four doses of each PDE5 inhibitor before considered non-responders.

The following are criteria-for-use to determine if a patient is a vardenafil non-responder. Vardenafil non-responders are to be offered a trial with a different PDE5 inhibitor. Patients who have previously responded to a different PDE5 inhibitor are to be offered treatment with that agent.

Patient has no concurrent drug interactions or is on stable alpha-blocker therapy	*Response*
1. Unable to achieve adequate response after 4 doses of vardenafil 20 mg 2. Unable to tolerate vardenafil dose titration to 20 mg and an inadequate response to 4 doses of a lower dose of vardenafil. 3. The provider or their representative has reviewed the proper use of vardenafil with respect to: o Timing of dosing o Use of sexual stimulation o Appropriate administration Note: If the provider finds any correctable problems with administration, the patient should be given a 4 dose re-trial at the maximum tolerated dose.	Meets 1 &3 or 2 & 3? ☐ Yes, Vardenafil non-responder ☐ No, retrial needed

Patients taking concurrent CYP3A4 Inhibitors	*Response*
CYP3A4 inhibitor — Max. dose vardenafil Ritonavir 2.5 mg/72 hrs Indinavir 2.5 mg/24 hrs Ketoconazole 400mg/day 2.5 mg/24 hrs Itraconazole 400 mg/day 2.5 mg/24 hrs Ketoconazole 200 mg/day 5 mg/24 hrs Itraconazole 200 mg/day 5 mg/24 hrs Erythromycin 5 mg/24 hrs 1. Unable to achieve adequate response after 4 doses. 2. Unable to tolerate vardenafil and an inadequate response to 4 doses of a lower dose of vardenafil (if possible). 3. The provider or their representative has reviewed the proper use of vardenafil with respect to: o Timing of dosing o Use of sexual stimulation o Appropriate administration Note: If the provider finds any correctable problems with administration, the patient should be given a 4 dose re-trial at the maximum recommended or tolerated dose.	Meets 1 &3 or 2 & 3? ☐ Yes, Vardenafil non-responder ☐ No, retrial needed
Patients taking Class IA or Class III antiarrhythmics or with congential or acquired QT prolongation	
	These patients should not receive vardenafil.

References:

1. Carson CC, Hatzichritou DG, Carrier S, et al. Erectile response with vardenafil in sildenafil nonresponders: a multicentre, double-blind, 12-week, flexible-dose, placebo-controlled erectile dysfunction clinical trial. BJU International 2004;94:1301-9.
2. Wespes E, Amar E, Hatzichristou D, et al. EAU guidelines on erectile dysfunction: An update. European Urology 2006;49:806-15.
3. VA Drug Class Review: Phosphodiesterase Type 5 Inhibitors available at: http://www.pbm.va.gov/reviews/PDE5InhibitorDrugClassReviewFinal12_27_05_2.pdf and http://vaww.pbm.va.gov/reviews/PDE5InhibitorDrugClassReviewFinal12_27_05_2.pdf

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